REMARKS

Status of the Claims

By virtue of the Listing of Claims presented herein, claims 1-3, 5-12, and 14-21 are pending. Claims 7 and 15-21 were withdrawn in a previous response, without prejudice or disclaimer, as directed to non-elected subject matter. Claim 1 has been herein amended to recite that the recited PYY or said PYY agonist for use in the claimed method is a peptide that comprises that comprises an active fragment of PYY. The amendment is made without prejudice or disclaimer to the right to pursue non-elected or deleted subject matter in one or more continuation or divisional applications. Basis for the amendment may be found, for example, at page 10, line 13, through page 11, line 11, which discloses that "PYY" may be selected form a peptide YY polypeptide obtained or derived from any species, and that a PYY analog may be selected from a polypeptide having an active fragment of PYY. Therefore, since the amendment introduces no new matter and places the claims in condition for allowance or better form for appeal, its entry is respectfully requested.

Claim Rejections

Applicants have carefully considered the points raised in the outstanding Office Action and believe that the Examiner's concerns have been addressed as described herein, thereby placing this case into condition for allowance.

Rejection under 35 U.S.C. § 112, first paragraph: written description

Claims 1-3, 5, 6, and 8-12 stand rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, the Examiner alleges that "the claims are drawn to a method comprising administration of PYY or a genus of structurally undefined PYY agonists," and that "the PYY encompassed by the claims are not limited to the peptide PYY mutants." From this the Examiner concludes that "the disclosed species are not representative of the entire genus." For the reasons previously made of record, which are herein incorporated by reference in their entirety, as well as the reasons set forth

below, this rejection is respectfully traversed.

The purpose behind the written description requirement is to ensure that the patent applicant had possession of the claimed subject mater at the time of filing of the application. *In re Wertheim*, 541 F.2d 257, 262, 191 USPQ 90, 96 (CCPA 1976). Further, a specification must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention, *i.e.*, whatever is now claimed. *Vas-Cath, Inc. v. Mahurkar*, 935 F.2d 1555, 1563-64, 19 USPQ.2d 1111, 1117 (Fed. Cir. 1991).

As mentioned in previous responses, the standard for determining whether a claim drawn to a genus meets the written description requirement is clear. "The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species, by actual reduction to practice . . . , reduction to drawings . . . , or by disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus." See *Regents of the University of California v. Eli Lilly,* 119 F.3d at 1568, 43 USPQ2d at 1406; M.P.E.P § 2163(II)(3)(a)(ii) (emphasis added).

What constitutes a "representative number" of species is an inverse function of the skill and knowledge in the art. *Capon v. Eshhar,* 418 F.3d 1349 (Fed. Cir. 2005). Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. Description of a representative number of species does not require the description to be of such specifics that it would provide individual support for each species that the genus embraces. "That is because the patent specification is written for a person of skill in the art, and such a person comes to the patent with the knowledge of what has come before. Placed in that context, it is unnecessary to spell out every detail of the invention in the specification; only enough must be included to convince a person of skill in the art that the inventor possessed the invention and to enable such a person to make and use the invention without undue experimentation." *Falkner*

v. Inglis, 448 F.3d, 1357, 1366 (Fed Cir. 2006). Additionally relevant to the analysis is the claimed invention, and the context of the genus encompassed by the claims.

As in *Capon* and *Falkner*, Applicants note that the instant claims are not drawn to a genus of compounds *per se*, but rather to novel uses of those compounds, based at least in part on the identification of functional and therapeutic attributes of those compounds, as recited in the instant treatment methods. Thus, the scope of the genus of PYY and PYY agonists is viewed in the context of the instantly claimed methods, and the disclosure of species within the genus is understood by those skilled in the art based on the scope of teachings related to the claimed methods. In this regard, Applicants note that the instant claims are directed to various methods of treating an intestinal damage comprising administering a pharmaceutically active formulation of PYY or a PYY agonist to a human to treat the intestinal damage. As amply disclosed throughout the instant application, administration of PYY or agonists thereof has an effect, for example to reduce intestinal damage, such as bowel atrophy, and to restore bowel mucosa or bowel function (see, e.g., page 6, lines 8-10; page 17, line 17, through page 20, line 17 (Example 1); FIGURE 2; and FIGURE 3). As stated in earlier responses, and as the artisan will recognize, the instant application and references incorporated therein in their entirety disclose numerous exemplary PYY and PYY agonists that comprise an active fragment of PYY, as recited in the instant claims, that may be selected by in order to practice the instantly claimed methods, *e.g.*, useful as agents to reduce intestinal damage, such as bowel atrophy, and to restore bowel mucosa or bowel function.

Thus there can be no doubt that, based on the scope of such teachings, the knowledge in the art, and the context of the claim invention, Applicants have provided more than adequate disclosure as to structural and functional characterization of PYY and PYY agonist polypeptides useful in the practicing the full scope of the instantly claimed methods. Accordingly, Applicants submit that PYY and PYY agonist polypeptides useful in the claimed methods are sufficiently described in the specification so to reasonably convey to one of ordinary skill in the art that the inventors, at the time the application was filed, had possession of the therapeutic methods of the claimed invention. As such, it is submitted that the claims comply with 35 U.S.C. §112, first paragraph, and reversal of this rejection is respectfully requested.

Rejection under 35 U.S.C. § 102(a)

Claims 1-3, 5, 10, and 13 stand rejected under 35 U.S.C. § 102(a) as being anticipated by El-Salhy et al. (El-Salhy et al., *Peptides*, Vol. 23, pp. 397-402 (February, 2002)). Specifically, the Examiner asserts that El-Salhy et al. teaches the following: "a decreased level of PYY in human patients with gastrointestinal disorders, including inflammatory bowel diseases (examples as Crohn's disease and ulcerative colitis; pages 398-399)"; that "changes in PYY in gastrointestinal disorders could be beneficial in clinical practice and in cases where PYY increase is desirable, diet that increases PYY synthesis and release can be followed, or a receptor agonist can be utilized"; that "infusion of PYY in dogs increases colonic absorption of water, Na, and Cl ions, and PYY or its analogue can be of use as clinical agents in intestinal malabsorption disorders or after bowel resection". From this, the Examiner concludes that El-Salhy teaches administration of PYY or PYY agonists to a subject, including a human, to treat intestinal damage."

As mentioned in previous responses, it is well established that to anticipate a claim, a reference must disclose every element of the claim. *Verdegaal Bros. v. Union Co. of California*, 2 U.S.P.Q.2d 1051, 1053 (Fed. Cir. 1987). Further, the identical invention must be shown in complete detail as is contained in the claim. *Richardson v. Suzuki Motor Co.*, 9 U.S.P.Q.2d 1913 (Fed. Cir. 1989). For the reasons previously made of record, which are herein incorporated by reference in their entirety, as well as the reasons set forth below, Applicant submits that cited prior art fails to disclose each and every element of the present claims, and therefore does not anticipate the instant claims.

The alleged teachings of the reference as outlined by the Examiner fail to teach or suggest any correlation between "a decrease in PYY levels in patients with gastrointestinal disorders, including inflammatory bowel diseases" and a therapeutic benefit that might be achieved by administering PYY or a PYY agonist to such patients, and certainly doest not teach that such a benefit comprises the treating intestinal damage that is associated with such disorders. Whereas the reference allegedly hypothesizes that "changes in PYY in gastrointestinal disorders could (Applicant's emphasis) be beneficial in clinical practice and in cases where PYY increase is desirable, diet that increases PYY synthesis and release can be

followed, or a receptor agonist can be utilized," such hypothesis fails to teach which particular changes (e.g., an increase, a decrease, etc.) would be beneficial in which particular "clinical practice," or how such particular changes might be exploited such that a therapy for such a "clinical practice" is achieved.

Indeed, the reference itself advertises the ambiguous, contradictory, and inconclusive nature of its alleged "teachings" throughout. For example, the reference opines that certain "changes in PYY seem to be an adaptive response to certain such disorders", whereas in other disorders, such changes in PYY "appear to be primary and could be one of the etiologic factors of [such] disease[s]" (Abstract). Further, whereas "the concentration of PYY in tissue extracts …of patients with Crohn's colitis and ulcerative colitis has been found to be lower than in controls (paragraph bridging pages 398 and 399)", "basal and postprandial plasma levels of PYY in these patients are elevated in patients (sic) with celiac disease" (page 399, second paragraph). Further still, whereas in one study performed in the author's laboratory "PYY cells have been found to be increased as compared to controls in the ascending colon of patients with CST [chronic idiopathic slow transit constipation]," another study performed in the same laboratory determined that "the number of colonic PYY cells has not been found to be affected," and whereas "the concentration of PYY in colonic tissue extracts from patients with CST has been reported to be high, basal and peak plasma PYY levels have been reported to be unaffected" (page 399, last paragraph).

> The confused nature of the report is perhaps most epitomized by its conclusion:
>
> The changes in PYY could be favorable in some intestinal disorders…[o]n the other hand, it could be harmful. The accumulated data of the changes in PYY in gastrointestinal disorders could be beneficial in clinical practice. Thus, in cases where PYY increase or decrease is desirable, diet that increases of decreases PYY synthesis and release can be used, or a receptor agonist or antagonist can be utilized.
> (page 402, last paragraph)

At best, the teachings of the reference merely reports the discordant aspect of the data accumulated with respect to PYY activity as it related to gastrointestinal disorders, and offers a invitation to rationalize this data such that a cohesive understanding as to PYY action in relation to the various "clinical practices" discussed might be achieved. It is simply a wish to invent.

The Examiner's assertion that the alleged teaching that infusion of PYY in dogs increases

colonic absorption of water, Na, and Cl ions is similarly unavailing, insofar as, at least, the dogs in the study did not have an intestinal damage associated with an inflammatory bowel disease (see references [38] and [39] as cited in El-Salhy et al.). Thus, this alleged teaching simply fails to offer any nexus between water and nutrient absorption in healthy doges and a method of treating any disorder or condition whatsoever. Therefore, and particularly in light of the contradictory and ambiguous nature or the data reported throughout the remainder of the reference, as mentioned above, this study certainly fails to teach or suggest to teach or suggest a method of treating intestinal damage comprising administering a pharmaceutically active formulation of PYY or a PYY agonist to a human in order to treat the intestinal damage, wherein said PYY or said PYY agonist is a polypeptide that comprises an active fragment of PYY, as instantly claimed.

In view or the foregoing, there can be no doubt that El-Salhy et al. fails to teach or suggest all of the elements of the instantly claimed methods, and in the complete detail as is contained therein. Accordingly, the rejection is in error and should be withdrawn.

Rejection under 35 U.S.C. § 102(b)

Claims 1, 2, 5, and 10-12 stand rejected under 35 U.S.C. § 102(b) as allegedly being anticipated by Balasubramaniam (U.S. Patent No. 5, 604, 203), hereinafter '203. Specifically, the Examiner maintains the assertion that '203 "clearly teaches administering PYY or a PYY agonist to a human," and teaches treating gastrointestinal disorders, especially infectious or inflammatory diarrhea, or diarrhea resulting from surgery," as well as Crohn's disease. From this, the Examiner concludes that '203 "teaches administering PYY to a subject to treat intestinal damages (sic) associated with these diseases." For the reasons previously made of record, which are herein incorporated by reference in their entirety, as well as the reasons set forth below, Applicant submits that cited prior art fails to disclose each and every element of the present claims, and therefore does not anticipate the instant claims.

Contrary to the Examiner's characterization of the reference, '203 does not teach or suggest a method of treating intestinal damage, or a method of treating intestinal damage associated with a condition, comprising administering a PYY or PYY agonist polypeptide in order to treat the intestinal damage, as instantly claimed. Indeed, for reasons similar to that

describe above, the reference fails to provide any nexus between the alleged effects of administration of the disclosed compounds on water and nutrient absorption, cell proliferation, and blood flow regulation and methods of treating intestinal damage comprising administering PYY or a PYY analog polypeptide, as instantly claimed. At best, the reference teaches that administration of the disclosed compounds may be useful in the treatment of "a number or gastrointestinal disorders…that are associated with excess intestinal electrolyte and water secretion as well as decreased absorption…" (column 7, line 1-7). The reference is absolutely silent with regard to a method of treating intestinal damage per se, and is similarly silent with regard to a method of treating intestinal damage that may be associated with the disorders disclosed in the reference. Indeed, the reference fails to teach or suggest that the disclosed disorders are accompanied by intestinal damage, and the Examiner has failed to demonstrate that that the alleged effects of administration of the disclosed compounds on water and nutrient absorption, cell proliferation, and blood flow regulation, constitute a teaching of a method of treating intestinal damage that might accompany the disclosed conditions. Thus, the reference does not teach a method of treating intestinal damage by administering a pharmaceutically active formulation of PYY or a PYY agonist to a human in order to treat the intestinal damage, wherein said PYY or said PYY agonist is a polypeptide that comprises an active fragment of PYY, as instantly claimed.

Therefore, there can be no doubt that '203 fails to teach or suggest all of the elements of the instantly claimed methods, and in the complete detail as is contained therein. Accordingly, the rejection is in error and should be withdrawn.

Rejection under 35 U.S.C. § 103(a)

The Examiner has rejected claim 14 under 35 U.S.C. § 103(a) as being allegedly unpatentable over Balasubramaniam (U.S. Patent No. 5, 604, 203), hereinafter '203, as applied to claims 1, 2, 5, and 10-12 above, and further in view of Dumont et al. 26:320-324 (1994). Specifically, the Examiner asserts that whereas '203 allegedly teaches a method of treating intestinal damage comprising administering a pharmaceutically active formulation of PYY or a PYY agonist to a human as applied to claims 1, 2, 5, and 10-12 above, '203 fails to teach the method of claim 14, comprising administering PYY[3-36]. The Examiner applies Dumont et al.

in an attempt to cure the deficiencies of '203. Applicant respectfully traverses.

For the reasons provided above, at least, '203 fails to teach a method of treating intestinal damage comprising administering a pharmaceutically active formulation of PYY or a PYY agonist polypeptide as instantly claimed. That Dumont et al. may teach that a PYY agonist, PYY[3-36], binds PYY receptors, as the Examiner contends, fails to cure the deficiencies of '203. Similar to that mentioned above, no nexus is provided linking alleged binding to PYY receptors to a method of treating intestinal damage per se, or in treating intestinal damage associated with the a condition or disorder, comprising administering a PYY or a PYY agonist polypeptide to treat the intestinal damage, as instantly claimed. Accordingly, the Section 103(a) rejection is in error and should be withdrawn.

In conclusion, all rejections outlined in the outstanding Office Action are in error and should be withdrawn.

Applicants believe that all issues raised in the Office Action have been properly addressed in this response and in the amendments to the claims as shown in the attached Listing of Claims. Accordingly, reconsideration and allowance of the amended claims is respectfully requested. If the Examiner feels that a telephone interview would serve to facilitate resolution of any outstanding issues, the examiner is encouraged to contact Applicants' representative at the telephone number below.

No additional fees are believed due for this submission. However, if a fee is due, the Commissioner is hereby authorized to charge payment of any fees associated with this communication, to Applicant's Deposit Account No. 010535 referencing Docket No. 0402US-UTL. Additionally, the Commissioner is hereby authorized to charge payment or credit overpayment of any fees during the pendency of this application to Applicant's Deposit Account No. 010535.

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Respectfully submitted,

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